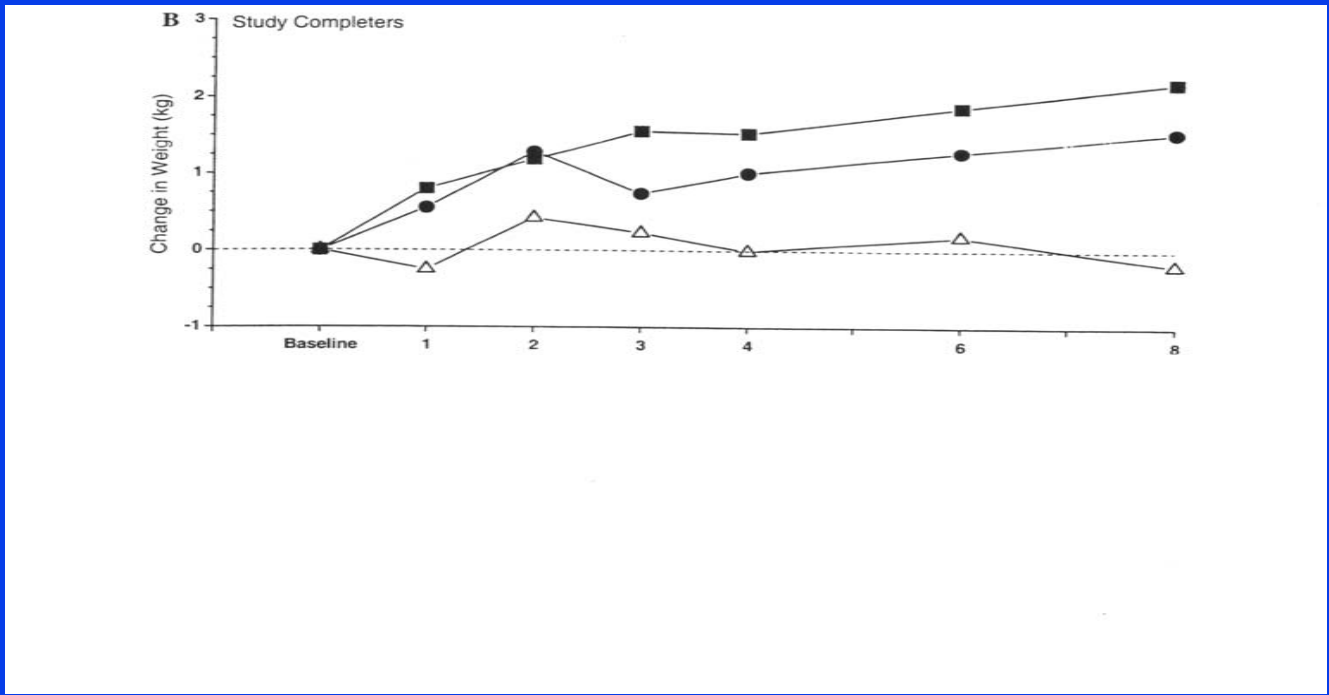
M_ss_ng D_t_a

Janet Wittes
Statistics Collaborative

The Caterpillar

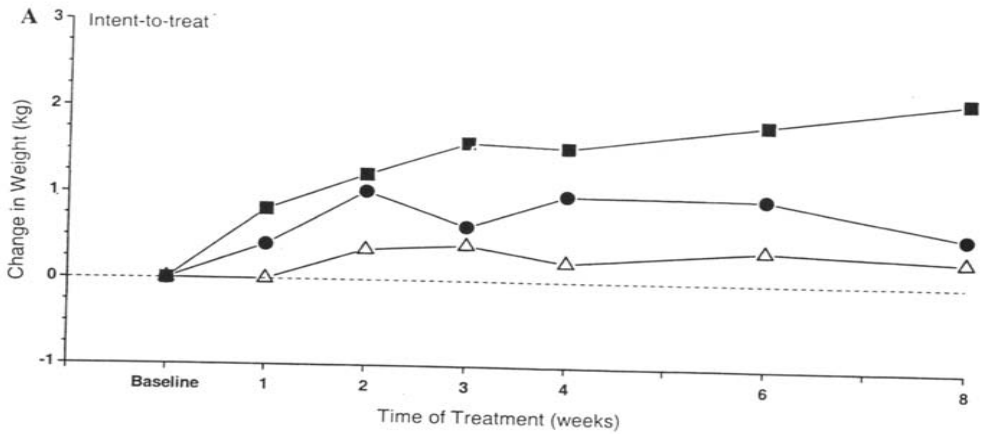
- Calling something the "intent-to-treat" population doesn't mean the analysis is "intent-to-treat"

Study Completers



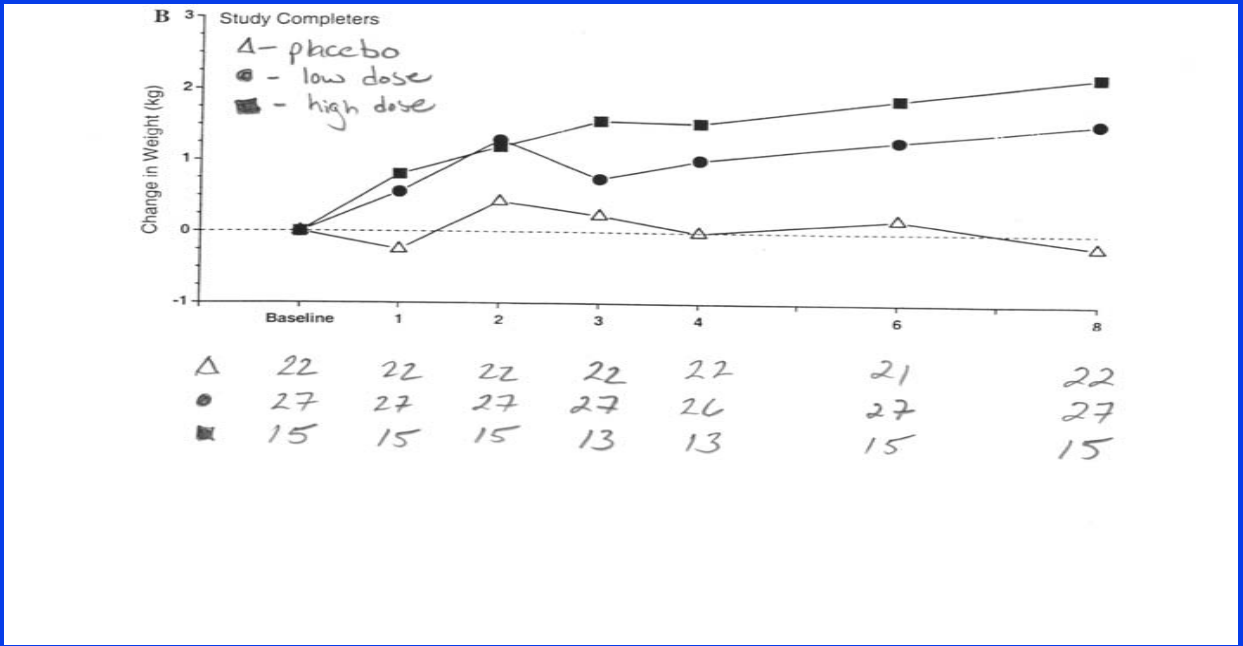
▲=placebo ■ =low ● =high

“Intent-to-treat”



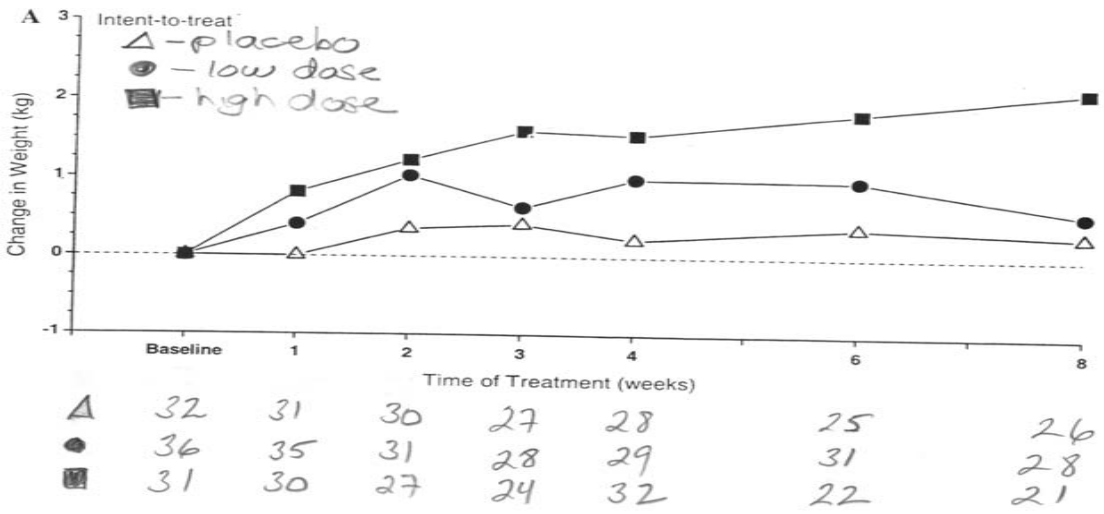
▲=placebo ■=low ●=high

Completers



▲=placebo ■ =low ● =high

"Intent-to-treat"



▲=placebo ■=low ●=high

Daily Mean Number of Urinary Incontinence Episodes

	Placebo	Behavior	Drug
Baseline	5.0 ± 3.2	4.8 ± 2.9	4.7 ± 2.9
Proportion missing final value			
	10%	12%	18%
Change to end of study			
LOCF	-2.1	-2.9	-3.2
Observed	-2.6	-2.8	-3.0

(n=100/group; all baseline medians=4)

Data collected

Completion of study/Withdrawal from study

Is the subject being withdrawn before the planned end of study? ..... N☐ No Y☐ Yes

If NO, please sign and date below and fill out only section "Completion of study".

If YES, please fill out the whole page.

Withdrawal from study

Date of withdrawal: __/__/2 0 0 (day) (month) (year)

Reason for premature withdrawal from study *(check only one)*

A☐ the subject no longer meets the criteria to remain in the study

B☐ new adverse event or worsening of an existing adverse event

Please supply an "Adverse event report" form as appropriate.

C☐ lack of efficacy

D☐ poor compliance with treatment

E☐ the subject did not wish to continue in the study

F☐ the subject is lost to follow-up

G☐ administrative reasons

H☐ protocol violation

I☐ the subject died

Please fax a "Serious adverse event report" and complete "In case of death" form.

L☐ at the discretion of the investigator

J☐ other reason *(please specify)* _____

Choices

- Don't have any missing values
- Use what you have
- Redefine your endpoint
- Use slope
- Impute
  - If so, how?

Avoid missing values

- Important to get follow-up measures
  - Cessation of program not excuse for failing to measure last observation

Use what you have

- Does not respect the randomization

Redefine your endpoint

- Ventilator failure in acute lung injury
  - Number of days ALIVE and not on ventilator
- Alcoholism
  - Number of days of known abstinence
  - Missing data = heavy drinking

Redefine…

- AIDS
  - Success=Known increase in weight of at least 1 kg
- Incontinence
  - Success= Known number of episodes less than 3 times per week

Slope

- Assume that slope extends beyond last measure
  - Even after death?

Impute

- Idea: assign number to the last value
- Choices
  - LOCF
  - Windows
  - Worst case
  - Worst reasonable case
  - Multiple imputation

What does it mean to impute?

- Reason for missing
  - Moved
  - Died
  - Adverse event
  - Quit

Classify your missing

- Completely at random
- At random
- Related to treatment

“Sensitivity” Analysis

- Do the conclusions vary depending on the method of analysis you use?

AIDS p-values vs. placebo

	Low dose	High dose
Completers	0.006	0.04
Still on original	0.0007	0.10
LOCF	0.012	0.40
Dawson/Lagakos	0.012	0.53
WRC	0.12	0.78
Multiple impute	0.045	0.31

Incontinence example

- How sure are we that
  - The drug works?
  - The behavioral intervention works?

Conclusion

- Think of how much missing data you will have
- Design study to minimize missing data
- In analysis, check how robust your analyses are